

Diagnosing and treating attention-deficit/hyperactivity disorder in adults

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Adult attention deficit/hyperactivity disorder (ADHD) is a valid and impairing psychiatric disorder. In this article, we review the diagnosis of ADHD in adults, focusing on symptom presentation differences between pediatric and adult ADHD as well as the importance of assessing functional impairments. Differentiating ADHD from other clinical disorders is often the most difficult part of making an ADHD diagnosis in adults. Psychiatric comorbidities are also described and discussed as potential impact factors upon not only diagnosing ADHD but also treatment of adult ADHD. Especially in those adults with psychiatric comorbidities, treatments need to be multimodal and include both pharmacotherapy and psychosocial interventions.

Key words: Attention-deficit/hyperactivity disorder, adult, comorbidity, stimulant medications, psychosocial interventions

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Over the past thirty years, there has been increasing recognition of the persistence of attention-deficit/hyperactivity disorder (ADHD) into adulthood. Once perceived to be exclusively a childhood disorder, it is now well accepted that about 4% of the adult population has ADHD (1-3). ADHD does not initially appear in adulthood. All valid diagnoses of adult ADHD have a clear developmental history of impairing symptoms dating back to childhood. However, it is possible that an individual may be initially *diagnosed* as having ADHD in adulthood (4). It is not uncommon to find adults self-referring themselves for an ADHD evaluation without having been diagnosed in childhood, and some data suggest that only 25% of adult ADHD cases had been diagnosed in childhood or adolescence (5).

This article provides an overview of the diagnosis, epidemiology and management of ADHD in adults.

DIAGNOSING ADHD IN ADULTS

Several sources of evidence show that ADHD can be diagnosed in a reliable and valid manner. Psychometric studies find clinician-administered ADHD rating scales to have high internal consistency and inter-rater reliability (6-8), and ADHD symptoms in adults are associated with clear signs of functional impairment (9-12). For screening purposes, a psychometrically validated self-report measure of adult ADHD is also available (8).

Despite substantial evidence for the validity of DSM diagnoses of ADHD, some questions remain regarding how the criteria are implemented when diagnosing adults, which requires a two stage process: a) determining that the adult met criteria for ADHD in childhood and b) determining that the adult currently meets criteria for the disorder. We will base our discussion on the DSM-IV-TR (13), which is the gold standard and most commonly applied method for diagnosing ADHD across the lifespan in the United States and is widely used in ADHD research around the world.

Diagnosing childhood onset ADHD in adults

When making the diagnosis of ADHD in adults, clinicians must establish that diagnostic criteria for the disorder were met in childhood. Because the passage of time may make symptoms difficult to recall, it is possible that the threshold for caseness should be lowered when making these retrospective diagnoses. But, as shown by Faraone and Biederman (6) in a population survey of 966 adults, lowering symptom thresholds can increase the risk for false positive diagnoses. They estimated a prevalence of 2.9% for narrow ADHD (meeting DSM-IV criteria in both childhood and adulthood) and 16.4% for broad ADHD (adding to that definition those meeting subthreshold criteria).

In a series of papers, Faraone et al (4,14,15) examined the validity of diagnosing ADHD in patients having impairing symptoms of ADHD which never exceeded DSM-IV's threshold for diagnosis (subthreshold ADHD). They evaluated the validity of these atypical diagnoses based on Robins and Guze's (16) criteria for the validity of psychiatric diagnoses, including clinical correlates, family history, treatment response, laboratory studies, course and outcome. They found that subthreshold ADHD had less psychiatric comorbidity, less neuropsychological dysfunction, and fewer substance use problems compared with full threshold ADHD. Moreover, the pattern of familial transmission for subthreshold ADHD differed from full threshold ADHD. These data suggested that cases of subthreshold ADHD should be viewed cautiously. Some might be a milder form of true ADHD, but others may be false positive diagnoses.

Several studies of youth have challenged the validity of the age at onset criterion (AOC) established by the DSM-IV for the diagnosis of ADHD (onset prior to age 7). One study comparing teenagers with onset before or after age 13 found no link between age at onset and severity of symptoms, types of adjustment difficulties, or the persistence of the disorder (17). Rohde et al (18) compared clinical features between adolescents meeting full criteria for ADHD and those meet-



ing all criteria except the AOC. Because these two groups had similar profiles of clinical features, the authors concluded that DSM-IV's age at onset criterion should be revised. In an epidemiologically ascertained sample of adolescents, Willoughby et al (19) found that adolescents meeting full criteria for combined type ADHD had worse clinical outcomes than those failing to meet the AOC, but found no differences attributable to the AOC for the inattentive subtype of ADHD. In the DSM-IV field trials, requiring an AOC of 7 reduced the accuracy of identifying currently impaired cases of ADHD and reduced agreement with clinician judgments (20). Hesslinger et al (21) found that adults with late onset ADHD had the same pattern of psychiatric comorbidity as adults whose ADHD onset met DSM-IV's criterion. In contrast, in an epidemiologic sample of 9 to 16 year old children, Willoughby et al (19) did not find late onset ADHD to be associated with oppositional defiant, conduct or anxiety disorders, while it was associated with depression among inattentive ADHD cases. In the series of papers by Faraone et al (4,14,15), late onset and full ADHD subjects had similar patterns of psychiatric comorbidity, neuropsychological impairment, substance use disorders and familial transmission. All of their late onset cases had onset in adolescence.

Taken together, studies of late onset ADHD suggest that the DSM's AOC is too low. Although these studies do not provide definitive evidence for a specific threshold, they clearly suggest that moving the AOC into adolescence (e.g., to 12 or 13) would be valid.

Diagnosing persistent ADHD in adults

After determining that the patient meets diagnostic criteria for ADHD in childhood, clinicians must determine if some of these symptoms have persisted into adulthood. When doing so, it is important to remember that the DSM-IV-TR criteria for ADHD allow the diagnoses to be made in adolescents and adults when only residual, impairing, symptoms of the disorder are evident. As Faraone et al's (22) review of longitudinal studies showed, about two-thirds of ADHD children will continue to have some impairing symptoms of ADHD in adulthood.

Barkley (23) has suggested that the DSM symptoms and symptom thresholds for ADHD are overly restrictive for diagnosing the disorder in adults. For example, he studied DSM symptom thresholds in two longitudinal samples followed into adulthood. As adults, 98% of their control participants endorsed three or fewer symptoms of inattention and 100% endorsed three or fewer of hyperactive impulsive behavior. In contrast, 100% of the ADHD group endorsed three or more inattention symptoms and 72% endorsed three or more hyperactive symptoms (23). These data suggest that six symptoms of inattention or hyperactivity (as required by the current DSM) is too high a threshold when diagnosing the current presence of ADHD in adults. However, when making a retrospective diagnosis about the oc-

currence of ADHD in childhood, the DSM threshold of six symptoms should be used (4,14,15).

In regards to symptom specificity and differentiating ADHD from other forms of psychopathology (e.g., mood disorders), Barkley (23) reported that symptoms of difficulty organizing tasks, having difficulty staying seated and talking excessively were equally prevalent in ADHD adults and adults with mood disorders or anxiety disorders. Three DSM-IV-TR inattentive symptoms correctly classified 87% of the ADHD group and 44% of the clinical control group: failing to give close attention to details; difficulty sustaining attention to tasks; failing to follow through on instructions. Three hyperactive/impulsive symptoms accurately classified 76% of ADHD cases and 49% of clinical control cases: fidgeting with hands/feet or squirms in seat; difficulty engaging in leisure quietly; interrupting or intruding on others.

Differentiating ADHD from other clinical disorders is often the most difficult part of making an ADHD diagnosis in adults, given the high comorbidity between ADHD and other psychiatric disorders (15). To further guide this differential diagnosis, Barkley (23) developed symptoms based upon his executive functioning theory of ADHD (24). The symptoms which best discriminated ADHD cases from those adults with other forms of psychopathology were: making decisions impulsively; having difficulty stopping activities or behavior when should do so; starting projects or tasks without reading or listening to directions carefully; poor follow through on promises; trouble doing things in their proper order; driving with excessive speed. These six items correctly classified ADHD with 85% accuracy (23). Making decisions impulsively and having difficulty stopping activities or behavior when one should were the best at discriminating adults with ADHD from adults with other forms of psychopathology. It is interesting that hyperactivity in adults may not distinguish adults with ADHD from normal adults or adults with other clinical disorders (23). As it is conceptualized now, however, hyperactivity is a core aspect of DSM-IV ADHD.

Assessing impairment in ADHD adults

While the relationship between symptoms and impairment in children with ADHD is modest ($r = .3$) (25), it may be more robust in adults ($r = .7$) (23). The DSM-IV-TR criterion C, which requires impairment in two or more settings, is central to the diagnosis of ADHD. It is essential that the diagnostic interview ask questions such as how is he/she doing at work, school, parenting, child-rearing, managing finances, driving, leisure time, and maintaining fulfilling relationships. The focus on functional impairments is central to the diagnosis of ADHD, most especially in an adult who does not have an ADHD diagnosis from childhood. Barkley's longitudinal data suggest that, in rank order from most to least impairing, educational impairments, home responsibilities, and occupational domains are the three most functionally impaired domains in adults with ADHD (23).





Unlike childhood disorders, in which the parents' and teachers' reports are frequently used, adult ADHD is often diagnosed with considerable or sole emphasis on self-report, because other informants are often not available. However, information from spouses, parents or other informants can be useful for several reasons, including the possibility of malingering symptoms for secondary gain (26). Similarly, given the positive illusory bias which has been documented in both children (27,28) and adults (29) with ADHD, it may be that adults with ADHD are not the best reporters of their own functioning. However, gaining collateral report from spouses, employers, coworkers, friends, etc. may be either difficult to obtain or clinically contraindicated. Nonetheless, we believe it should be obtained in a sensitive fashion whenever possible.

Diagnosing ADHD: primary care vs. psychiatry

Primary care physicians are increasingly being asked to make ADHD diagnoses. In a medical record review of 854 adults with persistent childhood-onset ADHD, Faraone et al (5) examined the diagnostic practices of primary care physicians and psychiatrists. They found that primary care physicians were less likely than psychiatrists to make an initial diagnosis of ADHD in adults if no pediatric ADHD diagnosis had been made. Primary care physicians were also more likely than psychiatrists to seek outside consultation before making an ADHD diagnosis in adults, with 15% of primary care physicians making a referral to another provider, most often a psychologist. Psychiatrists were also more likely to diagnose a comorbid psychiatric condition than primary care physicians (44% vs. 20% respectively).

EPIDEMIOLOGY OF ADHD IN ADULTS

National Comorbidity Survey Replication (NCS-R)

As discussed above, Faraone et al (6) computed a population prevalence of 2.9% for adult ADHD. Another estimate of population prevalence comes from the National Comorbidity Survey Replication (NCS-R) (3), an epidemiologic study of 9,200 adults ages 18-44. In this sample, the prevalence of adult ADHD was estimated to be 4.4%. Additional results indicated that adults with ADHD had lower educational levels, were less likely to be employed and were more likely to be separated/divorced than those without ADHD. ADHD was also less commonly reported in African-Americans and Latinos compared to Caucasians (3).

Fayyad et al (30) conducted an epidemiological study of adult ADHD in ten countries in the Americas, Europe and the Middle East. Their prevalence estimates ranged from 1.2 to 7.3%, with an average of 3.4%. The prevalence was lower in lower income (1.9%) compared with higher income countries (4.2%). Consistent with other studies, ADHD was associated with psychiatric comorbidity and functional impairment.

In children, ADHD is more commonly diagnosed in males (31). The NCS-R data suggest that sex differences are less pronounced in adult ADHD (3), which is consistent with data from clinical samples (4,32). The relative equal sex ratio in adult ADHD may indicate that ADHD in females is more persistent. It is also possible that this finding is due to referral biases in childhood: boys with ADHD are more likely to have conduct disorder and be referred for treatment (31). By being able to refer themselves, adults with ADHD may be less likely to have this referral bias.

Psychiatric comorbidity

Comorbid anxiety, mood and substance use disorders are commonly reported in adult ADHD (3,23,33-38). These comorbidity rates do not differ as a function of gender (3,39). The NCS-R data suggest that 43% of people with ADHD between 18 and 29 years of age experienced a psychiatric comorbidity, compared to 56% of those between 30 and 44 years of age.

In clinic-referred populations, histories of conduct disorder and oppositional defiant disorder occur in approximately 24-35% of adults with ADHD (1,35). This is lower than the rates often reported in pediatric ADHD (50-60%) (40). Alcohol use disorders are also common in clinic-referred adults with ADHD; alcohol dependence or abuse disorders lifetime prevalence rates range from 21 to 53% (1,15,35,41). Cannabis and cocaine use disorders are both also relatively common in adults with ADHD (42,43). Cigarette smoking has also been demonstrated to be more prevalent in adult ADHD (44). Comorbid conduct or bipolar disorder increases the risk for substance use disorders (45,46); however, ADHD is an independent risk factor for later substance use disorders (43,47). Those with comorbid ADHD and substance use disorders have been reported to have earlier onset of substance abuse relative to adults with substance abuse yet without ADHD (48) and a greater severity of substance abuse/dependence (49,50).

Mood disorders such as major depressive disorder occur in children with ADHD, especially those with conduct disorder (51). Between 16 and 31% of adults with ADHD have current comorbid major depressive disorder (1,3,23,35,41), with lifetime rates as high as 45% (3).

About 25% of children with ADHD have a comorbid anxiety disorder (40); rates of anxiety disorders in adult ADHD appear similar. For example, 25-43% of adults with ADHD meet criteria for generalized anxiety disorder (1,3,35,38,41), with lifetime rates as high as 59% (3). Panic disorder, obsessive compulsive disorder and social phobia are less common, yet can be comorbid conditions (3,38,52).

TREATING ADHD IN ADULTS

Despite the relatively high prevalence rate, the overwhelm-





ing majority of adults with ADHD are untreated; the NCS-R (3) demonstrated that only 11% of adults with ADHD are treated.

Pharmacotherapy

Stimulant medications, especially extended release formulations, are a front-line management strategy in both pediatric and adult ADHD (53,54). Approximately 3 of every 4 adults with ADHD will have a positive response to a stimulant medication. Two stimulants are FDA approved for use in ADHD adults: extended release mixed amphetamine salts and lisdexamfetamine dimesylate. Atomoxetine is a non-stimulant that is FDA approved for managing adult ADHD and may be particularly effective for adults with ADHD and comorbid depression (55) or for those with a comorbid substance use disorder addictive potential (56). Both the stimulants and atomoxetine improve core symptoms of hyperactivity, inattention and impulsivity (54,57,58). Secondary to psychiatric comorbidity, polypharmacy may be more likely in adult ADHD than pediatric ADHD (59).

Adherence to stimulant medications in ADHD wanes as a function of age (60), and efforts should be instituted to attempt to avert poor adherence. Stimulant misuse and/or diversion is another clinical reality in ADHD pharmacotherapy (61). Those with comorbid conduct disorder or substance abuse diagnoses are most at risk for stimulant misuse and/or diversion (61,62).

Psychosocial treatments

Substance use disorders may also require interventions, many of which may be independent of the ADHD interventions. Some have suggested that ADHD interventions should be initiated first to determine the extent to which ADHD is contributing to substance use disorders (23). The rationale for this is that the presence of ADHD appears to potentiate the substance use disorder, resulting in a more severe disorder (63) and poorer outcomes (64). However, because it can be very difficult to treat ADHD patients who are actively abusing alcohol or drugs, one must often treat the substance use disorder first. Given the potential for abuse or misuse of stimulant medications (65), in patients with a history of substance use disorders, one should use either long-acting stimulants (because their formulations make them less abusable) or a nonstimulant. The long-acting, prodrug stimulant, lisdexamfetamine dimesylate, is of particular interest given its lower abuse-related liking scores compared with equipotent doses of immediate-release d-amphetamine (58).

Similar to pediatric ADHD, a psychosocial treatment component is typically recommended in adult ADHD (66). What constitutes the psychosocial component, however, is different in adult ADHD relative to pediatric ADHD. For example, neither cognitive behavioral therapy (CBT) nor

cognitive therapy is effective for pediatric ADHD (67-71). In contrast, there are some data to suggest that CBT is efficacious for adults with ADHD. For example, in the adult ADHD literature, there is some evidence that CBT reduces functional impairments in adults concurrently treated with stimulants (72,73).

Treating ADHD: primary care vs. psychiatry

Psychiatrists are more likely than primary care physicians to prescribe a medication for adult ADHD (91% vs. 78% respectively) (5). While both psychiatrists and primary care physicians most often prescribed a stimulant (84%) or an antidepressant (12%), psychiatrists were more likely to prescribe dextroamphetamine, generic methylphenidate hydrochloride, mixed amphetamine salts, and oral osmotic controlled-release methylphenidate. Psychiatrists were less likely than primary care physicians to prescribe immediate release methylphenidate (5). Drug holidays were prescribed in approximately 20% of adults with ADHD, yet were more often prescribed by psychiatrists (24% vs. 17% respectively).

CONCLUSIONS

Within the last 30 years, the persistence of ADHD into adulthood has become increasingly well accepted, to the point that it is now considered a valid and impairing disorder. This suggests that the number of adults seeking clinical services for ADHD will likely continue to increase. Those working with adult populations need to be aware of the symptom presentation differences between pediatric and adult ADHD and the importance of assessing the functional impairments caused by ADHD symptoms.

Significant functional impairment and psychiatric comorbidity are the hallmark of adult ADHD. Especially in those adults with psychiatric comorbidities, treatments need to be multimodal and include both pharmacotherapy and psychosocial interventions.

References

1. Barkley RA, Murphy KR, Kwasnik D. Motor vehicle driving competencies and risks in teens and young adults with attention deficit hyperactivity disorder. *Pediatrics* 1996;98:1089-95.
2. Heiligenstein E, Conyers LM, Berns AR et al. Preliminary normative data on DSM-IV attention deficit hyperactivity disorder in college students. *J Am Coll Health* 1998;46:185-8.
3. Kessler RC, Adler L, Barkley R et al. The prevalence and correlates of adult ADHD in the United States: results from the National Comorbidity Survey Replication. *Am J Psychiatry* 2006;163:716-23.
4. Faraone SV, Biederman J, Spencer T et al. Diagnosing adult attention deficit hyperactivity disorder: are late onset and subthreshold diagnoses valid? *Am J Psychiatry* 2006;163:1720-9.
5. Faraone SV, Spencer TJ, Montano CB, et al. Attention-deficit/hyperactivity disorder in adults: a survey of current practice in psychiatry and primary care. *Arch Intern Med* 2004;164:1221-6.





6. Faraone SV, Biederman J. What is the prevalence of adult ADHD? Results of a population screen of 966 adults. *J Atten Disord* 2005; 9:384-91.
7. Adler LA, Faraone SV, Spencer TJ et al. The reliability and validity of self- and investigator ratings of ADHD in adults. *J Atten Disord* 2008;11:711-9.
8. Adler LA, Spencer T, Faraone SV et al. Validity of pilot adult ADHD self report scale (ASRS) to rate adult ADHD symptoms. *Ann Clin Psychiatry* 2006;18:145-8.
9. Mick E, Spencer T, Faraone SV et al. Assessing the validity of the Quality of Life Enjoyment and Satisfaction Questionnaire Short Form in adults with ADHD. *J Atten Disord* 2008;11:504-9.
10. Biederman J, Petty CR, Fried R et al. Stability of executive function deficits into young adult years: a prospective longitudinal follow-up study of grown up males with ADHD. *Acta Psychiatr Scand* 2007; 116:129-36.
11. Biederman J, Petty C, Fried R et al. Impact of psychometrically-defined executive function deficits in adults with ADHD. *Am J Psychiatry* 2006;163:1730-8.
12. Biederman J, Faraone SV, Spencer T et al. Functional impairments in adults with self-reports of diagnosed ADHD: a controlled study of 1001 adults in the community. *J Clin Psychiatry* 2006;67:524-40.
13. American Psychiatric Association. Diagnostic and statistical manual of mental disorders, 4th ed, text revision. Washington: American Psychiatric Association, 2000.
14. Faraone SV, Biederman J, Doyle AE et al. Neuropsychological studies of late onset and subthreshold diagnoses of adult ADHD. *Biol Psychiatry* 2006;60:1081-7.
15. Faraone SV, Wilens TE, Petty C et al. Substance use among ADHD adults: implications of late onset and subthreshold diagnoses. *Am J Addict* 2007;16(Suppl. 1):24-34.
16. Robins E, Guze SB. Establishment of diagnostic validity in psychiatric illness: its application to schizophrenia. *Am J Psychiatry* 1970; 126:983-87.
17. Schaughency E, McGee R, Raja SN et al. Self reported inattention, impulsivity and hyperactivity at ages 15 and 18 in the general population. *J Am Acad Child Adolesc Psychiatry* 1994;33:173-84.
18. Rohde LA, Biederman J, Zimmermann H et al. Exploring ADHD age-of-onset criterion in Brazilian adolescents. *Eur Child Adolesc Psychiatry* 2000;9:212-8.
19. Willoughby MT, Curran PJ, Costello EJ et al. Implications of early versus late onset of attention-deficit/hyperactivity disorder symptoms. *J Am Acad Child Adolesc Psychiatry* 2000;39:1512-9.
20. Applegate B, Lahey B, Hart E et al. Validity of the age of onset criterion for attention-deficit/hyperactivity disorder: a report from the DSM-IV field trials. *J Am Acad Child Adolesc Psychiatry* 1997; 36:1211-21.
21. Hesslinger B, Tebartz van Elst L, Mochan F et al. Attention deficit hyperactivity disorder in adults-early vs. late onset in a retrospective study. *Psychiatry Res* 2003;119:217-23.
22. Faraone S, Biederman J, Mick E. The age dependent decline of attention-deficit/hyperactivity disorder: a meta-analysis of follow-up studies. *Psychol Med* 2006;36:159-65.
23. Barkley R, Murphy K, Fischer M. ADHD in adults: what the science says. New York: Guilford, 2007.
24. Barkley RA. Behavioral inhibition, sustained attention, and executive functions: constructing a unifying theory of ADHD. *Psychol Bull* 1997;121:65-94.
25. Gordon M, Antshel K, Faraone S et al. Symptoms versus impairment: the case for respecting DSM-IV's criterion D. *J Atten Disord* 2006;9:465-75.
26. Harrison AG, Edwards MJ, Parker KC. Identifying students faking ADHD: preliminary findings and strategies for detection. *Arch Clin Neuropsychol* 2007;22:577-88.
27. Gerdes AC, Hoza B, Pelham WE. Attention-deficit/hyperactivity disorder boys' relationships with their mothers and fathers: child, mother, and father perceptions. *Dev Psychopathol* 2003;15:363-82.
28. Hoza B, Pelham WE Jr, Dobbs J et al. Do boys with attention-deficit/hyperactivity disorder have positive illusory self-concepts? *J Abnorm Psychol* 2002;111:268-78.
29. Knouse LE, Bagwell CL, Barkley RA et al. Accuracy of self-evaluation in adults with ADHD: evidence from a driving study. *J Atten Disord* 2005;8:221-34.
30. Payyad J, De Graaf R, Kessler R et al. Cross-national prevalence and correlates of adult attention-deficit hyperactivity disorder. *Br J Psychiatry* 2007;190:402-9.
31. Gaub M, Carlson CL. Gender differences in ADHD: a meta-analysis and critical review. *J Am Acad Child Adolesc Psychiatry* 1997; 36:1036-45.
32. Biederman J, Faraone SV, Monuteaux MC et al. Gender effects on attention-deficit/hyperactivity disorder in adults, revisited. *Biol Psychiatry* 2004;55:692-700.
33. Borland BL, Heckman HK. Hyperactive boys and their brothers: a 25-year follow-up study. *Arch Gen Psychiatry* 1976;33:669-75.
34. Morrison JR. Adult psychiatric disorders in parents of hyperactive children. *Am J Psychiatry* 1980;137:825-7.
35. Biederman J, Faraone SV, Spencer T et al. Patterns of psychiatric comorbidity, cognition, and psychosocial functioning in adults with attention deficit hyperactivity disorder. *Am J Psychiatry* 1993;150: 1792-8.
36. Heiligenstein E, Guenther G, Levy A et al. Psychological and academic functioning in college students with attention deficit hyperactivity disorder. *J Am Coll Health* 1999;47:181-5.
37. Murphy K, Barkley RA. Attention deficit hyperactivity disorder adults: comorbidities and adaptive impairments. *Compr Psychiatry* 1996;37:393-401.
38. Shekim WO, Asarnow RF, Hess E et al. A clinical and demographic profile of a sample of adults with attention deficit hyperactivity disorder, residual state. *Compr Psychiatry* 1990;31:416-25.
39. Biederman J, Faraone SV, Spencer T et al. Gender differences in a sample of adults with attention deficit hyperactivity disorder. *Psychiatry Res* 1994;53:13-29.
40. MTA Collaborative Group. A 14-month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder. The MTA Cooperative Group. Multimodal Treatment Study of Children with ADHD. *Arch Gen Psychiatry* 1999;56:1073-86.
41. Mannuzza S, Klein RG, Bessler A et al. Adult outcome of hyperactive boys. Educational achievement, occupational rank, and psychiatric status. *Arch Gen Psychiatry* 1993;50:565-76.
42. Wilens T. Attention-deficit/hyperactivity disorder and the substance use disorders: the nature of the relationship, subtypes at risk and treatment issues. *Psychiatr Clin North Am* 2004;27:283-301.
43. Biederman J, Wilens T, Mick E et al. Psychoactive substance use disorder in adults with attention deficit hyperactivity disorder: effects of ADHD and psychiatric comorbidity. *Am J Psychiatry* 1995;152:1652-8.
44. Kollins SH, McClernon FJ, Fuemmeler BF. Association between smoking and attention-deficit/hyperactivity disorder symptoms in a population-based sample of young adults. *Arch Gen Psychiatry* 2005;62:1142-7.
45. Mannuzza S, Klein RG, Bessler A et al. Adult outcome of hyperactive boys: educational achievement, occupational rank and psychiatric status. *Arch Gen Psychiatry* 1993;50:565-76.
46. Weiss G, Hechtman L, Milroy T et al. Psychiatric status of hyperactives as adults: a controlled prospective 15-year follow-up of 63 hyperactive children. *J Am Acad Child Adolesc Psychiatry* 1985;24: 211-20.
47. Molina B, Pelham W. Childhood predictors of adolescent substance use in a longitudinal study of children with ADHD. *J Abnorm Psychol* 2003;112:497-507.
48. Wilens T, Biederman J, Abrantes AM et al. Clinical characteristics of psychiatrically referred adolescent outpatients with substance use disorder. *J Am Acad Child Adolesc Psychiatry* 1997;36:941-7.
49. Carroll K, Rounsaville B. History and significance of childhood at-





- tention deficit disorder in treatment-seeking cocaine abusers. *Compr Psychiatry* 1993;34:75-82.
50. Schubiner H, Tzelepis A, Milberger S et al. Prevalence of attention-deficit/hyperactivity disorder and conduct disorder among substance abusers. *J Clin Psychiatry* 2000;61:244-51.
 51. Angold A, Costello EJ, Erkanli A. Comorbidity. *J Child Psychol Psychiatry* 1999;40:57-87.
 52. Torgersen T, Gjervan B, Rasmussen K. ADHD in adults: a study of clinical characteristics, impairment and comorbidity. *Nord J Psychiatry* 2006;60:38-43.
 53. Pliszka S. Practice parameter for the assessment and treatment of children and adolescents with attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry* 2007;46:894-921.
 54. Faraone SV, Spencer T, Aleardi M et al. Meta-analysis of the efficacy of methylphenidate for treating adult attention deficit hyperactivity disorder. *J Clin Psychopharmacol* 2004;54:24-9.
 55. Spencer TJ, Faraone SV, Michelson D et al. Atomoxetine and adult attention-deficit/hyperactivity disorder: the effects of comorbidity. *J Clin Psychiatry* 2006;67:415-20.
 56. Wee S, Woolverton WL. Evaluation of the reinforcing effects of atomoxetine in monkeys: comparison to methylphenidate and desipramine. *Drug Alcohol Depend* 2004;75:271-6.
 57. Michelson D, Adler L, Spencer T et al. Atomoxetine in adults with ADHD: two randomized, placebo-controlled studies. *Biol Psychiatry* 2003;53:112-20.
 58. Faraone SV. Lisdexamfetamine dimesylate: the first prodrug stimulant treatment for ADHD. *Expert Opin Pharmacother* (in press).
 59. Spencer TJ. Advances in the treatment of adult ADHD. In: *New perspectives on adult ADHD - Recognizing impairment, improving lives*, Vol. 6. Boston: Haymarket Medical Education, 2007:1-4.
 60. Charach A, Ickowicz A, Schachar R. Stimulant treatment over five years: adherence, effectiveness, and adverse effects. *J Am Acad Child Adolesc Psychiatry* 2004;43:559-67.
 61. Wilens TE, Adler LA, Adams J et al. Misuse and diversion of stimulants prescribed for ADHD: a systematic review of the literature. *J Am Acad Child Adolesc Psychiatry* 2008;47:21-31.
 62. Gordon SM, Tulak F, Troncale J. Prevalence and characteristics of adolescents patients with co-occurring ADHD and substance dependence. *J Addict Dis* 2004;23:31-40.
 63. Wilens TE, Biederman J, Mick E. Does ADHD affect the course of substance abuse? Findings from a sample of adults with and without ADHD. *Am J Addict* 1998;7:156-63.
 64. Ercan ES, Coskunol H, Varan A et al. Childhood attention deficit/hyperactivity disorder and alcohol dependence: a 1-year follow-up. *Alcohol Alcohol* 2003;38:352-6.
 65. Faraone SV, Wilens TE. Effect of stimulant medications on later substance use and the potential for misuse, abuse, and diversion. *J Clin Psychiatry* 2007;68(Suppl. 11):15-22.
 66. Dodson WW. Pharmacotherapy of adult ADHD. *J Clin Psychol* 2005;61:589-606.
 67. Abikoff H, Gittelman R. Hyperactive children treated with stimulants. Is cognitive training a useful adjunct? *Arch Gen Psychiatry* 1985;42:953-61.
 68. DuPaul GJ, Eckert TL. The effects of school-based interventions for attention deficit hyperactivity disorder: a meta-analysis. *School Psychology Digest* 1997;26:5-27.
 69. Dush DM, Hirt ML, Schroeder HE. Self-statement modification in the treatment of child behavior disorders: a meta-analysis. *Psychol Bull* 1989;106:97-106.
 70. Baer RA, Nietzel MT. Cognitive and behavioral treatment of impulsivity in children: a meta-analytic review of the outcome literature. *J Clin Child Psychol* 1991;20:400-12.
 71. Bloomquist ML, August GJ, Ostrander R. Effects of a school-based cognitive-behavioral intervention for ADHD children. *J Abnorm Child Psychol* 1991;19:591-605.
 72. Safren SA, Otto MW, Sprich S et al. Cognitive-behavioral therapy for ADHD in medication-treated adults with continued symptoms. *Behav Res Ther* 2005;43:831-42.
 73. Rostain AL, Ramsay JR. A combined treatment approach for adults with ADHD - results of an open study of 43 patients. *J Atten Disord* 2006;10:150-9.